

**This Page Is Inserted by IFW Operations
and is not a part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- **BLACK BORDERS**
- **TEXT CUT OFF AT TOP, BOTTOM OR SIDES**
- **FADED TEXT**
- **ILLEGIBLE TEXT**
- **SKEWED/SLANTED IMAGES**
- **COLORED PHOTOS**
- **BLACK OR VERY BLACK AND WHITE DARK PHOTOS**
- **GRAY SCALE DOCUMENTS**

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

CLAIMS

- 5 1. A nucleic acid molecule encoding a VEGF-X protein or a functional equivalent, derivative or bioprecursor thereof, said protein comprising any of the sequences from position 23 to 345 of the amino acid sequence illustrated in Figure 10, or the complete sequence as illustrated in Figure 10.
- 10 2. A nucleic acid molecule according to claim 1 wherein said nucleic acid is a DNA molecule.
- 15 3. A nucleic acid molecule according to claim 1 wherein said nucleic acid is a cDNA molecule.
- 20 4. A nucleic acid molecule according to claim 3 comprising the nucleotide sequence from position 257 to 1291 of the nucleotide sequence illustrated in Figure 9, or sequences that hybridise thereto under high stringency conditions or the complement thereto.
- 25 5. An antisense molecule capable of hybridising to a molecule according to claim 1 under high stringency conditions.
- 30 6. A nucleic acid molecule according to claim 1 which is of mammalian origin.
7. A nucleic acid molecule according to claim 6 which is of human origin.
- 35 8. An isolated VEGF-X protein, or a functional equivalent, derivative or bioprecursor thereof, having an amino acid sequence from position 23 to 345 of the amino acid sequence illustrated in Figure 10 or the complete amino acid sequence of Figure 10.

657499460

Sub
B5

Sub
B6

9. A VEGF-X protein, or a functional equivalent, derivative or bioprecursor thereof, encoded by a nucleic acid molecule as defined in claim 1.

5 10. A protein according to claim 9, which comprises the amino acid sequence illustrated in Figure 10.

See B7
11. An expression vector comprising a nucleic acid molecule according to claim 1.

10 12. An expression vector according to claim 11 further comprising a nucleotide sequence encoding a reporter molecule.

15 13. An expression vector comprising an antisense molecule according to claim 5.

14. A nucleic acid molecule according to claim 1 for use as a medicament.

20 15. A host cell transformed or transfected with an expression vector according to claim 11 or 12.

25 16. A host cell transformed or transfected with an expression vector according to claim 13.

17. A transgenic cell, tissue or organism comprising a transgene capable of expressing a VEGF-X protein according to claim 8 or 9.

30 18. A transgenic cell, tissue or organism according to claim 17, wherein said transgene is included in an expression vector.

35 19. A VEGF-X protein or a functional equivalent, derivative or bioprecursor thereof, expressed by a cell according to claim 15.

66727 4493460

20. A VEGF-X protein, or a functional equivalent, derivative or bioprecursor thereof, expressed by a transgenic cell, tissue or organism according to claim 17.

5

See
B8

10

21. A process for producing a VEGF-X protein according to claim 8, said process comprising transforming a host cell or organism with an expression vector according to claim 11, and recovering the expressed protein from said host cell or organism.

15

22. An antibody capable of binding to a protein according to claim 8, or an epitope thereof.

23. An antibody according to claim 22 for use as a medicament.

20

24. A pharmaceutical composition comprising an antibody according to claim 22 together with a pharmaceutically acceptable carrier diluent or excipient thereof.

25

25. A method of identifying VEGF-X protein in a sample which method comprises contacting said sample with an antibody according to claim 22 and monitoring for binding of any protein to said antibody.

30

26. A kit for identifying the presence of VEGF-X protein in a sample which comprises an antibody according to claim 22 and means for contacting said antibody with said sample.

35

27. A method of identifying compounds which modulate angiogenesis which method comprises providing a host cell or organism according to claim 15 or a transgenic cell, tissue or organism according to

094634460

claim 17, contacting a test compound with said cell,
tissue or organism and monitoring for an effect of
said compound on said VEGF compared to a host cell or
organism according to claim 15 or a transgenic cell
tissue or organism which has not been contacted with
said compound.

28. A compound identifiable according to the method
of claim 27.

29. A compound according to claim 28 for use as a
medicament.

30. A nucleic acid sequence comprising the
nucleotide sequences illustrated in any of Figures 3,
5, 8 or 13.

31. A method for producing a polypeptide, said
method comprising the steps of:

- a) culturing the host cell of claim 15 under
conditions suitable for expression of the
polypeptide; and
- b) recovering the polypeptide from the host
cell culture.

32. A method of inhibiting angiogenic activity and
inappropriate vascularisation including formation and
proliferation of new blood vessels, growth and
development of tissues, tissue regeneration and organ
and tissue repair in a subject said method comprising
administering to said subject an amount of an
antisense molecule according to claim 5 in sufficient
concentration to reduce or prevent said angiogenic
activity.

33. A method of inhibiting angiogenic activity or

inappropriate vascularisation including any of
formation and proliferation of new blood vessels,
growth and development of tissues, tissue
regeneration and organ and tissue repair in a subject
5 said method comprising administering to said subject
an amount of an antibody according to ~~claim~~ 22 in
sufficient concentration to reduce or prevent said
angiogenic activity or inappropriate vascularisation.

10 34. A method of inhibiting angiogenic activity or
inappropriate vascularisation including any of
formation and proliferation of new blood vessels,
growth and development of tissues, tissue
regeneration and organ and tissue repair in a
15 subject, said method comprising implanting in said
subject cells that express an antibody according to
claim 22.

20 35. A method of treating or preventing any of
cancer, rheumatoid arthritis, psoriasis and diabetic
retinopathy, said method comprising administering to
said subject an amount of an antisense molecule
according to ~~claim~~ 5 in sufficient concentration to
treat or prevent said disorders.

25 36. A method of treating or preventing any of
cancer, rheumatoid arthritis, psoriasis and diabetic
retinopathy, said method comprising administering to
said ~~subject~~ an amount of an antibody according to
30 claim 22 in sufficient concentration to reduce or
prevent said disorders.

35 37. A method of promoting angiogenic activity or
vascularisation to promote wound healing, skin graft
growth, tissue repair, proliferation of new blood
vessels, tissue regeneration and organ repair which
method comprises applying or delivering to a site of

SECRET 499450

interest a therapeutically effective amount of any of
a group selected from a protein according to claim 8
and a nucleic acid molecule encoding a VEGF-X protein
or a functional equivalent, derivative or
5 bioprecursor thereof comprising an amino acid
sequence illustrated in Figure 10, an expression
vector comprising said nucleic acid molecule and a
pharmaceutical composition comprising any of said
nucleic acid molecule and said protein.

10

38. A method of treating wounds selected from the
group consisting of dermal ulcers, pressure sores,
venous sores, diabetic ulcers and burns by applying
to said wound a therapeutically effective amount of
15 any of a VEGF-X protein according to claim 8, a
pharmaceutical composition comprising said protein
and a pharmaceutically acceptable carrier, diluent or
excipient therefor.

20

39. A nucleic acid molecule encoding a polypeptide
having a CUB domain said polypeptide comprising the
amino acid sequence from position 40 to 150 of the
sequence of Figure 10.

25

40. A nucleic acid molecule encoding a polypeptide
having a CUB domain, said polypeptide comprising the
amino acid sequence of Figure 26.

30

41. A nucleic acid molecule according to claim 40,
comprising the nucleotide sequence from position 5 to
508 of the sequence illustrated in Figure 26.

35

42. A nucleic acid molecule according to claim 41
comprising the nucleotide sequence illustrated in
Figure 26.

43. A nucleic acid molecule encoding a VEGF like

65 75 85 95 105 115 125 135 145 155 165 175 185 195 205 215 225 235 245 255 265 275 285 295 305 315 325 335 345 355 365 375 385 395 405 415 425 435 445 455 465 475 485 495 505 515 525 535 545 555 565 575 585 595 605 615 625 635 645 655 665 675 685 695 705 715 725 735 745 755 765 775 785 795 805 815 825 835 845 855 865 875 885 895 905 915 925 935 945 955 965 975 985 995

See
BIO

domain comprising the sequence from position 214-345 of the sequence of Figure 10 or the sequence from position 15 to 461 illustrated in Figure 24.

5 44. An expression vector comprising a nucleic acid molecule according to claim 39 or 40.

10 45. An expression vector comprising a nucleic acid molecule according to claim 43.

15 46. A host cell transformed or transfected with an expression vector according to claim 44.

20 47. A host cell transformed or transfected with an expression vector according to claim 45.

25 48. A protein expressed by the cell according to claim 46.

30 49. A protein expressed by the cell according to claim 47.

35 50. A method of identifying compounds that inhibit or enhance angiogenic activity, said method comprising contacting a cell expressing a VEGF receptor and/or a neuropilin 1 or 2 type receptor with said compound in the presence of a VEGF-X protein according to claim 8 and monitoring for the effect of said compound or said cell when compared to a cell which has not been contacted with said compound.

51. A compound identifiable according to the method of claim 50 as an inhibitor or enhancer of angiogenic activity.

52. A method of inhibiting angiogenic activity or

657227-2400460

See
BIO
art

inappropriate vascularisation, said method comprising contacting a cell expressing a VEGF receptor and a neuropilin type receptor with a protein selected from any of a protein according to claim 8 and a protein according to claim 48 or a protein according to claim 49.

53. Use of a nucleotide sequence illustrated in any of Figures 14 and 15 in identifying a VEGF-X protein according to claim 8.

54. A nucleic acid molecule encoding a polypeptide comprising a CUB domain having the sequence from position 40 to 150 of the sequence of Figure 10 or from position 5 to 508 of the sequence of Figure 26 and a sequence encoding a VEGF domain.

55. A nucleic acid molecule according to claim 54 wherein said sequence encoding said VEGF domain is selected from the sequences encoding any of VEGF A to D or isoforms or variants thereof.

56. A nucleic acid molecule encoding a polypeptide comprising the amino acid sequence from position 40 to 150 of the sequence illustrated in Figure 10 for use as a medicament.

57. Use of a nucleic acid molecule encoding a polypeptide having the amino acid sequence from position 40 to 150 of the sequence illustrated in Figure 10 in the manufacture of a medicament for treatment of disease conditions associated with inappropriate angiogenesis such as tumour or cancer growth, retinopathy, osteoarthritis or psoriasis.

58. A polypeptide comprising the amino acid sequence from position 40 to 150 of the sequence illustrated

557-337-4493-60

See
B11

in figure 10 for use as a medicament.

59. A polypeptide comprising the amino acid sequence from position 40 to 150 of the sequence illustrated in Figure 10 in the manufacture of a medicament for the treatment of disease conditions associated with inappropriate angiogenesis such as tumour growth, retinopathy, osteoarthritis or psoriasis.

60. Use of a CUB domain comprising the amino acid sequence from position 40 to 150 of the sequence of Figure 10, or the amino acid sequence of Figure 26, to identify compounds which inhibit angiogenic activity in a method according to claim 50.

61. A method of inhibiting angiogenic activity and inappropriate vascularisation including formation and proliferation of new blood vessels, growth and development of tissues, tissue regeneration and organ and tissue repair in a subject said method comprising administering to said subject an amount of a polypeptide having an amino acid sequence from position 40 to 150 of the sequence illustrated in Figure 10 or a nucleic acid molecule according to any of claims 39 to 42 in sufficient concentration to reduce or prevent said angiogenic activity.

62. A method of treating or preventing any of cancer, rheumatoid arthritis, psoriasis and diabetic retinopathy, said method comprising administering to said subject an amount of a polypeptide having an amino acid sequence from position 40 to 150 of the sequence illustrated in Figure 10 or a nucleic acid molecule according to any of claims 39 to 42 in sufficient concentration to treat or prevent said disorders.

63. An antisense molecule capable of hybridising to a molecule according to claim 39 under high stringency conditions.
- 5 64. An antisense molecule capable of hybridising to a molecule according to claim 43 under high stringency conditions.
- 10 65. A transgenic cell, tissue or organism comprising a transgene capable of expressing a protein according to claim 48.
- 15 66. A transgenic cell, tissue or organism comprising a transgene capable of expressing a protein according to claim 49.
- 20 67. A transgenic, cell tissue or organism according to claim 65 or 66, wherein said transgene is included in an expression vector according to claim 41 or 42.
- 25 68. An antibody capable of binding to a protein according to claim 48 or an epitope thereof.
69. An antibody capable of binding to a protein according to claim 49 or an epitope thereof.
- 30 70. A pharmaceutical composition comprising an antibody according to claim 68 or 69 together with a pharmaceutically acceptable carrier diluent or excipient therefor.
- 35 71. A pharmaceutical composition comprising a compound according to claim 48 together with a pharmaceutically acceptable carrier, diluent or excipient therefor.

SECRET 433460

See
B12

72. A nucleic acid molecule encoding a variant of a VEGF-X protein having any of the sequences of nucleotides illustrated in Figure 12.

Add C3

044334 499450